## REMARKS

Claims 1-7, 12, 31 and 44-46 were pending in the present application. Claim 1 has been amended and claims 45-46 have been canceled. The remarks made herein are designed to place the case in condition for allowance. As such, Applicants respectfully request that the remarks made herein be entered and fully considered.

## Rejection of Claims 1-7, 12, 31 and 44-46 Under 35 U.S.C. § 101 and §112

Claims 1-7, 12, 31 and 44-46 remain rejected under 35 U.S.C. §101 because "[t]he claimed invention is not supported by a credible, substantial, specific, or well-established utility."

Applicants respectfully traverse this rejection and submit that an asserted specific, substantial and credible utility has been set forth in the application as filed. For the reasons discussed below, reconsideration of the rejection is requested.

The Examiner maintained the rejection under 35 U.S.C. §101 for the following reasons: 1) the Examiner agrees that the TANGO 405 molecule of the present application is a C-type lectin, however the Examiner states that C-type lectins exhibit diverse functions; 2) the Examiner states that no patentable utility has been established for murine dectin-2 and therefore Applicants' assertion that TANGO 405 has a well-established utility based on sequence homology to murine dectin-2 is void; and 3) the Examiner states that Applicants assertion of utility is not specific or substantial because the present application never discloses any utility directly and specifically associated with the claimed TANGO 405. Applicants address each of these rejections below.

I. Human TANGO 405 is a member of the dectin family of C-type lectins

As stated on page 49 of the specification, human TANGO 405 was isolated from a human mixed lymphocyte reaction cDNA library. A mixed lymphocyte reaction involves culturing lymphocyte populations from two individuals, where T cells recognize the foreign cells and become activated and proliferate. This proliferation is due to the disparity in the MHC class II antigens and T cells from one individual which interact with the MHC class II antigen bearing cells from the other individual, such as B cells, dendritic cells and langerhans cells. Therefore, a

cDNA library which is generated using a mixed lymphocyte reaction will be composed of activated T cells, B cells, dendritic cells and langerhans cells. Applicants' specification additionally discloses on page 53 that the murine dectin-2 gene was isolated from dendritic cells, that human TANGO 405 is 89% identical to murine dectin-2 and that TANGO 405 is the human orthologue of murine dectin-2 (refer to lines 9-10, 14-15 and 23-24 of page 53). As established in the response filed to the June 14, 2004 Office Action, the human TANGO 405 molecule of the present invention was confirmed by Kanazawa et al. (refer to citation B2 in Supplemental Information Disclosure Statement (IDS) filed December 14, 2004) to be the human orthologue of murine dectin-2. Kanazawa et al. additionally confirm that human dectin 2 is expressed on dendritic cells. Therefore, contrary to the Examiner's assertion, Applicants' disclosure is specific as Applicants have stated that, not only is TANGO 405 a C-type lectin, but that it belongs to a small family of molecules within the C-type lectin family known as dectins. As described below, Applicants' disclosure provides utilities which are specific to dectins and not, as asserted by the Examiner, diverse functions related to all C-type lectins.

II. Murine dectin-2 has a well established utility

Applicants disclose that murine dectin 2 is expressed by murine dendritic cells and is involved in the activation of naïve T cells (refer to page 56, lines 35-36 of specification). In fact, Dr. Kiyoshi Ariizumi of the University of Texas Southwestern Medical Center, who has published numerous papers on the dectin family of molecules, has confirmed that dectin 2 is required for dendritic cell-mediated T cell activation (refer to the University of Texas Southwestern Faculty Profile abstract submitted herewith as citation B4 in the Supplemental IDS). Dr. Ariizumi additionally concludes that dectin 1 and 2 are members of the costimulatory family of molecules, which are known to be responsible for inducing T cell activation and proliferation, and therefore modulation of these molecules may regulate immune reactions and tumor recognition. Again, Applicants disclose at page 57, lines 11-20 of the specification, that TANGO 405 proteins are involved in disorders relating to aberrant lymphocyte activation and proliferation. Applicants then provide examples of such disorders and state that modulation of the activity or expression of TANGO 405 can be used to diagnose or treat such disorders. This is

directly in line with the teachings of Dr. Ariizumi. Applicants therefore submit that murine dectin 2 has a well-established, utility as an activator of T cells.

III. Human TANGO 405 has a specific and substantial utility

The Examiner further rejected Applicants' argument that the present situation is analogous to that provided in Example 10 of the Utility Guidelines, stating that "[i]n the enzyme world, functional property is much more predictable based on sequence homology." Applicants respectfully disagree. Not only is the present situation completely analogous to the ligase example provided in Example 10 of the Utility Guidelines, but Applicants have provided evidence that Applicants were correct in describing the human TANGO 405 as the human orthologue of the murine dectin 2 (see above). Certainly if the Utility Guidelines allow for prediction of function based on high sequence identity levels between molecules within the same species, then the same should hold true for molecules determined to be orthologues based on high sequence identity levels. Therefore, if one identifies a human molecule that is highly identical to a characterized molecule of another species, enough so to characterize the human molecule as the human orthologue, such as in the present situation, then one can expect that the two molecules will have the same function, much like enzymes that have been determined to be family members based on homology. Hence, as established above, Applicants had disclosed that murine dectin 2 was involved in activation of naïve T cells, which has been further corroborated by Dr. Ariizumi (refer to citation B4 in the enclosed Supplemental IDS). Based on the fact that Applicants disclosed that human TANGO 405 is the human orthologue of murine dectin 2 and the fact that murine dectin 2 is involved in the activation of naïve T cells, Applicants' disclosure further provides specific and substantial utilities for human TANGO 405, such as modulating T cell-mediated immune responses (see page 57, line 1 of specification). Contrary to the Examiner's arguments that "[i]mmune response encompasses many types of responses with distinct natures, and *activating or inhibiting* are mutually exclusive utilities" (refer to page 3, lines 3-4 of Office Action), Applicants submit that the disclosure on page 57 of the specification is specific to the "lymphocyte *activating* capacities" of TANGO 405.

Therefore, in summary, Applicants have isolated a human C-type lectin from a mixed lymphocyte cDNA library, which contains activated T cells and dendritic cells, and called this molecule TANGO 405. Applicants additionally disclose that TANGO 405 is the human orthologue of murine dectin-2 and have provided evidence confirming that TANGO 405 is indeed the human orthologue of murine dectin 2. Applicants further disclose that murine dectin 2 is involved in activation of naïve T cells, which again, has been further substantiated (see above). Applicants have therefore asserted that *human* TANGO 405 is involved in, for example, immune responses, i.e. T cell-mediated immune responses. Applicants submit that this asserted utility is a well established, credible and substantial utility. Therefore, Applicants respectfully request reconsideration and withdrawal of the foregoing 35 U.S.C. § 101 rejection over claims 1-7, 12, 31 and 44.

**Rejection of Claims 1-7, 12, 31 and 44-46 Under 35 U.S.C. §112, first paragraph**

Claims 1-7, 12, 31 and 44-46 are rejected under 35 U.S.C. §112, first paragraph. Specifically, the Examiner has maintained the argument that one skilled in the art would not know how to use the claimed invention since the claimed invention is not supported by either a credible asserted utility or a well established utility.

Applicants respectfully traverse this rejection. As discussed above in response to the utility rejection, the claimed invention does have a credible asserted utility, and as such one of skill in the art would be able to make and use the claimed invention.

**Rejection of Claims 1-7, 12, 31 and 44-46 Under 35 U.S.C. §112, first paragraph**

Claims 1-7, 12, 31 and 44-46 remain rejected under 35 U.S.C. §112, first paragraph, enablement, over the recitation of sequence variants and fragments.

Applicants respectfully traverse this rejection, however in the interest of expediting prosecution, and in no way acquiescing to the Examiner's rejection, Applicants have i) amended claim 1a) to change 90% to 95% and ii) deleted claim 1c), 45 and 46.

This limitation within new claim 1a) is fully enabled within the specification as Applicants have provided teachings for every element needed for one of skill in the art to practice

the claimed invention.

First, Applicants have provided which regions of the sequence of SEQ ID NOs:51 and 52 can be altered and still encode a functional TANGO 405 polypeptide. Specifically, Applicants have taught several domains and regions within the TANGO 405 polypeptide which are conserved and essential for activity of the polypeptide, namely the i) C-type lectin domain signature sequence at amino acids 176 to 202 of SEQ ID NO:53; and ii) the C-type lectin domain at amino acids 105 to 202 of SEQ ID NO:53 (refer to, for example, table VII on page 51 of the specification and Figure 4). Applicants additionally provide an alignment between the amino acid sequence of TANGO 405 (SEQ ID NO:53) and murine dctin 2 (refer to Figure 4M). By having identified the regions necessary for activity, Applicants have taught which regions of the polypeptide are amenable to alterations as well as those which are not amenable to alterations.

Second, the specification teaches one how to generate functional variants by performing conservative substitutions within the TANGO 405 molecule of the invention. As defined on page 72, lines 2-4 of the specification, a "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain." The Applicants have also defined which of the amino acids have similar side chains, thereby providing a skilled artisan the necessary tools to generate functional variants of the polypeptide used in the claimed invention.

Finally, Applicants have provided teachings for one of skill in the art to be able to perform assays to determine whether or not specific sequences have the ability to modulate a TANGO 405 activity. Such activities can include, for example, the ability to modulate growth, proliferation, survival or differentiation of cells which express TANGO 405, for example, lymphocytes (refer to page 56, lines 9-15). Based on these activities, one can perform assays on specific sequences to determine whether or not such sequences can, for example, modulate the proliferation of T cells as compared to a control. Performing assays to determine whether or not a variant having at least 95% identity to the sequence of SEQ ID NOs:51 or 52 has the desired properties would not constitute undue experimentation.

Therefore, Applicants have provided all of the necessary information to enable one of skill in the art to 1) identify regions within the TANGO 405 molecule of the present invention

which may be altered while maintaining activity; 2) generate variants having at least 95% identity to the sequence of SEQ ID NOs:51 or 52, and 3) perform assays to determine whether or not the sequences generated do in fact have the desired TANGO 405 activity.

Therefore, contrary to the Examiner's assertions, Applicants have provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of claims 1-7, 12, 31 and 44. Therefore, Applicants respectfully request reconsideration and withdrawal of the foregoing 35 U.S.C. § 112, first paragraph rejection over claims 1-7, 12, 31 and 44.

## CONCLUSION

In view of the amendments and remarks made herein, Applicants respectfully submit that the rejections presented by the Examiner are now overcome and that this application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is believed that this paper is being filed timely and that a three month extension of time is required. In the event any additional extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

| | |
|---|---|
| October 19, 2005 | MILLENNIUM PHARMACEUTICALS, INC.<br>By  <br>Mario Cloutier<br>Registration No.: 57,225<br>40 Lansdowne Street<br>Cambridge, MA 02139<br>Telephone – (617) 577-3522<br>Facsimile – (617) 551-8820 |